Pertussis/Parapertussis

Communicable Disease Control Unit

Case Definition

Confirmed Case: Isolation of *Bordetella pertussis* or *Bordetella parapertussis* on culture from an appropriate clinical specimen (1, 2) or positive polymerase chain reaction (PCR) assay for *B. pertussis*/*B. parapertussis* (2).

OR

A person who is epidemiologically linked to a laboratory-confirmed case and has one or more of the following for which there is no other known cause:

- paroxysmal cough of any duration
- cough ending in vomiting or associated with apnea
- cough with inspiratory "whoop" (2)

Clinical/Probable Case: A person having a cough of ≥ two weeks duration in the absence of appropriate laboratory tests and who is not epidemiologically linked to a laboratory-confirmed case and has one or both of the following with no other known cause:

- paroxysmal cough
- inspiratory "whoop" (2, 3)

Reporting Requirements

- All clinical specimens positive for *Bordetella pertussis* or *Bordetella parapertussis* are reportable by laboratory[1] to the Director of Communicable Disease Control, Manitoba Health.
- All clinical cases are reportable by the attending health care professional to the Director of Communicable Disease Control, Manitoba Health.
- Confirmed cases are referred to Public Health for follow-up.
- Operators of clinical laboratories in Manitoba that are isolating *B. pertussis* or *B. parapertussis* from clinical specimens must submit isolate subcultures to the Cadham Provincial Laboratory (CPL) for subtyping, susceptibility testing and epidemiologic investigation.

Clinical Presentation/Natural History

Pertussis, also known as whooping cough, is a respiratory infection caused by the bacterium *Bordetella pertussis* (1). Unlike other infections, the bacteria usually remain on the surface of the airways and do not invade the tissues (1). Intracellular *B. pertussis* organisms have been found in clinical specimens; however, their significance in transmission and pathophysiology, if any, remains unknown (5). Pertussis antigens appear to allow the organism to evade host defenses. Lymphocytosis occurs, but chemotaxis is impaired (3). The disease interferes with the normal transfer of mucus from the airways to the mouth, leading to attacks of coughing (1). Dissemination of the organism beyond the respiratory tract has not been documented (5). Severity of disease is greatest among young infants (4). The disease is divided into three stages (catarrhal, paroxysmal and convalescent) (3, 5-7):

1) **Catarrhal Stage –** The first stage begins about seven to 10 days after infection (6, 7), and is characterized by runny nose, sneezing, low-grade fever and a mild occasional cough similar to the common cold (6).
2) **Paroxysmal Stage –** This stage occurs 10 to 14 days after infection (6). The frequency and severity of coughing with paroxysms increases rapidly (6, 7). Paroxysms are characterized by repeated

1 Except during outbreaks, laboratories continue to be the greatest source of pertussis reporting (4).

violent coughs; each series of paroxysms has many coughs without intervening inhalation and can be followed by a crowing or high-pitched inspiratory whoop. The patient may become cyanotic (3). Paroxysms frequently end with the expulsion of clear, tenacious mucus, often followed by vomiting (8). Paroxysms may be more frequent at night and may be precipitated by external stimuli such as noises, cold air, eating, drinking, crying and laughing (1, 5). Individuals may appear well between paroxysms (5, 6). Individuals with partial immunity may experience less severe symptoms (3). The paroxysmal stage usually lasts one to six weeks but may persist for up to 10 weeks (3).

3) **Convalescent Stage –** Recovery is gradual with cough becoming less paroxysmal and disappearing in two to three weeks (3). A typical illness lasts six to 12 weeks in total (1).

Complications are most common in infants (under 12 months of age) (9). Secondary bacterial pneumonia is the most common complication and the cause of most pertussis-related deaths (3). Pneumonia may be caused by *B. pertussis* or by other organisms (5). Less common complications include seizures and encephalopathy (3, 9). Minor complications include ear infections, nosebleeds and small conjunctival hemorrhages as a result of forceful coughing (1).

Roughly 20 to 30 per cent of infants with pertussis are admitted to hospital (1). About one of every 400 infants hospitalized with pertussis dies as a result of either pneumonia or brain damage (1). With the introduction of acellular vaccine, the annual number of hospital-admitted cases has gradually declined (4). There are fewer vaccine failures and increased effectiveness in preschool-aged children (4).

Parapertussis is a milder version of whooping cough and is caused by a similar bacterium called *Bordetella parapertussis* (6). A similar acute clinical syndrome characterized by a self-limited reactive airways disease (asthma) has been reported in association with viruses, especially adenoviruses; however, the duration of cough is usually less than 28 days (10).

Etiology

Pertussis is caused by the bacterium *Bordetella pertussis*, a small aerobic gram-negative coccobacillus that appears singly or in pairs (7, 11). *Bordetella parapertussis* causes the milder disease parapertussis (6). *Bordetella bronchiseptica*, an animal pathogen, can in rare instances cause difficult-to-treat respiratory infections in humans (7).

Epidemiology

Reservoir and Source: Humans are believed to be the only host for pertussis (8, 11). Although infections can be induced in animals in a laboratory setting, there are no known natural infections of animals or animal reservoirs (5). The organism is unable to survive for long periods in the environment (5). Adolescents and adults are an important reservoir for *B. pertussis* and are frequently the source of infection for susceptible infants (3, 12-15).

Transmission: The spread of pertussis requires close, direct contact such as droplets expelled from the respiratory tract of infected persons landing in the nose or mouth of susceptible persons (1, 6). The number of organisms required for infection is unknown (5). Transmission occurs less often by contact with recently contaminated articles of an infected person (3). Asymptomatic chronic carriers of *B. pertussis* are uncommon (14, 15), and are unlikely to be a significant source of infection because they are not coughing (5).

Occurrence:

General: Pertussis is endemic worldwide, particularly in young children regardless of ethnicity, climate or geographic location (8). Outbreaks occur periodically every three to five years (5). The mechanism of this periodic pattern is unknown (5); however, it has been speculated that epidemics are the result of an

accumulation of susceptible persons in a population between cycles (5). The World Health Organization (WHO) estimated that about 17.6 million cases of pertussis occurred worldwide in 2003, of which 90 per cent were in developing countries (14). There were about 279,000 deaths from the disease in 2003 (14). Since the end of the 1980s, about 80 per cent of all infants worldwide have received pertussis vaccine (14).

In recent years, Australia, Canada, the United States and several European countries have seen an increase in the incidence of pertussis, particularly among older children and adults (15). In some countries the epidemiological shift is unequivocal (14). In the youngest age group, failure to maintain high primary immunization is thought to be the major cause of increased pertussis incidence (15). Much of the increased incidence of pertussis in the older groups however, is believed to be the result of waning immunity, improved laboratory diagnosis, stronger surveillance and greater notification (14-16). It is believed that there is still substantial under-reporting of pertussis, especially in adults (9, 13, 15). So far, developing countries have not reported increased incidence of pertussis in adolescents and adults nor have industrialized countries with low immunization coverage (14, 15).

Canada: The epidemiology of pertussis in Canada is shifting from preschool-aged children to adolescents and adults (4). Differences in disease burden across jurisdictions are more likely related to the adequacy and intensity of surveillance (4). The number of reported cases in Canada has increased from the early 1990s, with peaks occurring every four years (9). The highest incidence has been among infants. The second highest rate occurred among the 10 to 14-year age group (9). Possible reasons for the increasing incidence include low efficacy of the whole cell vaccine used, waning vaccine immunity, a decrease in vaccination coverage, a change in circulating strains of *B. pertussis* and increased awareness and reporting (9). As the reporting of pertussis in Canada is believed to be highly underestimated, it is difficult to come up with an accurate estimate (17, 18). The incidence rate of pertussis has remained between 9.5 and 35 per 100,000 per year between 1991 and 2002, with an average of 5,720 cases reported each year (19). Almost two-thirds of reported cases occur between July and December, peaking between August and October (1). Pertussis kills between one and three infants every year in Canada (1).

Manitoba: There were 82 reported cases (seven per 100,000) of pertussis in 2004 (20). Of these cases, 35 per cent occurred in the 10 to14-year age group, while 18 per cent occurred in the infant group (20). In 2005, 34 cases of pertussis (three per 100,000) were reported with 38 per cent of cases occurring in the infant group and 32 per cent of cases occurring in the 10 to 14-year age group (20). No deaths were reported in 2004 or 2005 (20).

Incubation: The average incubation period for pertussis is seven to 10 days; however, incubation can range from six to 20 days (1, 5, 8).

Host Susceptibility and Resistance: The susceptibility of non-immunized individuals is universal (8). Transplacental immunity in infants has not been demonstrated (8). Although *B. pertussis* can infect people of all ages, infants appear to be the most susceptible (17, 21). Milder and atypical cases occur in all age groups (8). Immunity following *B. pertussis* natural infection or induced by whole-cell vaccination (currently, only the acellular vaccine is used in Canada) is not life-long (22, 23). Several recent studies have indicated a higher incidence of pertussis in females than in males in the adolescent and adult categories (21-24).

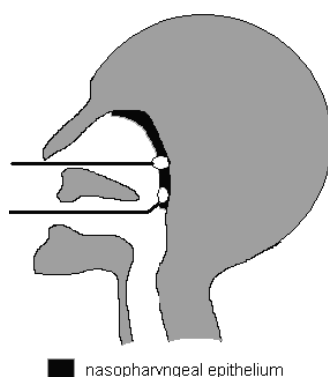
Period of Communicability: Individuals with pertussis are most infectious during the catarrhal stage and the beginning of the paroxysmal stage (first two weeks after onset of symptoms) (1, 3, 8, 14). Infectiousness declines quickly after this period but may last up to three weeks in untreated patients

(1, 8, 14, 25). Patients are no longer considered infectious after five days of treatment with appropriate antibiotics (1, 8, 25). Pertussis has a secondary attack rate of 80 per cent among susceptible household contacts (3).

Diagnosis

Culture: Diagnosis is based on culture of *B. pertussis* from nasopharyngeal specimens obtained during the catarrhal and early paroxysmal stages of disease (14). Success in isolating *B. pertussis* is reduced with prior antibiotic therapy effective against pertussis, in vaccinated persons, and if specimen collection is delayed beyond the first two weeks of illness (3, 26). Nasopharyngeal specimens may be obtained by;

- Nasal aspirate – collect by fine flexible plastic catheter connected to a syringe and deposit in a sterile container (preferred sample). This method provides a larger sample which can be used for culture and PCR (27, 28).
- Posterior nasopharynx – pass a flexible swab[2] through the nares to the posterior nasopharynx (Figure 1).
- Posterior pharynx to nasopharynx – insert a flexible swab[2] through the mouth up into the posterior pharynx and collect specimen from posterior nasopharynx (Figure 1).

Figure 1. Collection of pharyngeal/nasopharyngeal specimen

The swabs should be plated as soon as possible onto selective media (3). Negative cultures do not necessarily exclude pertussis as the cause of disease, especially in vaccinated children or when the cough has been present for greater than two to three weeks (18).

PCR (Polymerase Chain Reaction): PCR has been accepted nationally in Canada as evidence of laboratory confirmation of pertussis since May 2000 (21); however, it may not be routinely available (29). Currently, PCR should be used in addition to rather than as a replacement for culture as bacterial isolates may be required for evaluation of antimicrobial resistance or for molecular typing (3, 4). PCR may be able to detect the organism at a later stage of the infection, when the ability to culture declines (22). Non-viable organisms can still be detected (5) by PCR, but they cannot be distinguished from viable organisms (27). PCR can be helpful for the differentiation of *B. pertussis* and *B. parapertussis* colonies (27).

Direct Fluorescent Antibody (FA) Staining: Direct FA staining of nasopharyngeal secretions is not recommended due to frequent false-positive and false-negative results (8, 28).

Serology: Serological diagnosis is based on the detection of a significant change in the level of specific antibodies in paired sera of infected individuals (14). Results of serological testing are difficult to interpret due to a lack of association of antibody levels and immunity to pertussis and because it is not yet standardized (3). There is no consensus on the protective antibody levels or on the role of different types of antibodies in protection against disease (30). Serological testing is not useful for diagnosing acute infection, but is useful in establishing a diagnosis retrospectively (31). During the year following vaccination, serology based on single sera cannot be used for diagnosis as it may not differentiate between antibodies following natural infection and

2 Calgi (calcium alginate) or Dacron swabs should be used for culture as cotton inhibits the growth of the organism (5). Dacron or rayon swabs are preferred for PCR (not calcium-alginate swabs) (4, 29).

antibodies resulting from vaccination (14). Serology can be the most important diagnostic tool in adolescents and adults, because pertussis is often diagnosed late in these individuals and they are frequently culture-negative (27).

Strikingly high total WBC counts with a strong preponderance of lymphocytes are found as the whooping stage develops, although this may not occur in young infants (10) or in patients with *B. parapertussis* infection (32).

Key Investigations

- Contact history
- Antimicrobial history
- Immunization history

Control

Management of Cases

Treatment: Macrolide antibiotics such as azithromycin and erythromycin may prevent or moderate clinical pertussis when given during the incubation period or in the early catarrhal stage (1). During the paroxysmal phase of the disease, antibiotics may not shorten the clinical course but may reduce the possibility of complications (6). Antibiotics eliminate the organism after a few days of use and thus reduce transmission (14, 33).

The following antimicrobials are indicated (adapted from the National Consensus Conference on Pertussis) (9):

- Azithromycin
  - Children: 10 mg/kg (maximum 500 mg) once daily for one day, then five mg/kg (maximum 250 mg) once daily for four days (9);
  - Adults: 500 mg on day one, then 250 mg once daily for four days.
- Clarithromycin
  - Children: 15 mg/kg per day (maximum one g/day) orally, in two divided doses for seven days (9, 32);
  - Adults: 500 mg twice daily (maximum one g/day) for seven days (35).
- Erythromycin [estolate preparation preferred (9, 34)]
  - Children: 40-50 mg/kg per day (maximum one g/day), orally in four divided doses for seven to 10 days (10);
  - Adults: 500 mg orally four times daily for seven days (35).

Recent evidence has shown azithromycin to be as effective as erythromycin for treatment of pertussis in children, with fewer gastrointestinal adverse events and greater compliance (34). Azithromycin is considerably more expensive than erythromycin and cost may influence treatment choice (34).

Infants younger than two months of age who are receiving macrolide antibiotics should be monitored for symptoms and signs of pyloric stenosis (9).

Cotrimoxazole can be used if erythromycin is not tolerated (9).

Pregnant women with catarrh and/or cough suggestive of early pertussis should be treated with erythromycin (10). The estolate preparation is contraindicated in pregnancy (36). If treatment is not tolerated or not completed by time of delivery, it should be given post-delivery to both mother and newborn. There is no need to isolate the infant from the mother (10).

Infants younger than six months of age and other patients with severe disease commonly require hospitalization for supportive care to manage complications (32). When heavy vomiting occurs, fluids and electrolytes may need to be replaced intravenously (6). For infants, it may be necessary to suck out mucus with a vacuum device or install a nasal breathing tube to help breathing (6). Extra oxygen may also be required (6).

Public Health Measures

- For hospitalized cases, Routine Practices and Droplet Precautions are recommended for five days after initiation of effective therapy or until three weeks

after the onset of paroxysms if appropriate antimicrobial therapy is not given (32).

- Exclusion is not a proven effective strategy; however, in high-risk situations (where there are vulnerable[3] persons) exclusion until five days after the start of antibiotic therapy, or if no treatment is given, until after 21 days with negative results from culture or PCR should be at the discretion of the Medical Officer of Health (9).

Management of Contacts

Definition of Contact: Someone who has:

- had direct face-to-face exposure for five or more minutes with a symptomatic case-patient (in the catarrhal or paroxysmal period of illness) (10, 36).
- shared confined space in close proximity (household, day care, office) for a prolonged period of time such as one hour or longer, with a symptomatic case-patient (36).
- had direct contact with respiratory, oral or nasal secretions from a symptomatic case-patient such as kissing, being directly coughed or sneezed upon or sharing food or eating utensils during a meal (10, 36).

Regional health authority staff will identify all contacts requiring chemoprophylaxis and refer them to their physician for prescriptions (10).

Chemoprophylaxis of Contacts

- May be warranted as pertussis immunity is not absolute and immunization may not prevent infection (32).
- When indicated is the same antibiotic regimen described in the **Treatment** section.
- Since pertussis is more severe in newborns, infants and young children, age of the contact should be considered before implementing chemoprophylaxis (10).
- Initiating chemoprophylaxis after 21 days or more following the onset of cough in the primary case is unlikely to be beneficial (9).
- There is no evidence that antibiotic prophylaxis of contacts changes the epidemic course of pertussis in the community (37); therefore, it is recommended only for the following situations.

1) Households and Home Day Cares

- Chemoprophylaxis is indicated for contacts (vaccinated against pertussis or not), **ONLY** where there is a vulnerable person residing/working or in attendance (9).
- Children younger than seven years of age should have their immunization status reviewed and updated, if appropriate (9, 10, 32) (see *Canadian Immunization Guide*).

2) Non-Home Day Cares/Schools

- Contacts should be offered chemoprophylaxis **ONLY** if they are a vulnerable person (10).
- Contacts younger than seven years of age should have their immunizations reviewed and updated, if necessary (10) (see *Canadian Immunization Guide*).

3) Community

- Includes contacts in situations other than those described above.
- Contacts who are vulnerable persons should receive chemoprophylaxis (10).
- Children younger than seven years of age should have their immunizations reviewed and updated, if appropriate (10) (see *Canadian Immunization Guide*).

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3 A vulnerable person is defined as an infant under one year of age (vaccinated or not); or a pregnant woman in her third trimester (9).

Manitoba Health and the National Advisory Committee on Immunization (NACI) recommend that children seven years of age or older, who are unimmunized or incompletely immunized (including children whose immunization status is unknown), receive the Tdap vaccine (tetanus with reduced diphtheria toxoid and pertussis components). The first two doses of Tdap should be at four to eight-week intervals, the third dose six to 12 months later, followed by a booster 10 years later. Use of Tdap in children seven years of age or older will require the health care provider to obtain informed consent and disclose the fact that the product is currently not licensed for this age group but is still recommended by Manitoba Health and NACI (38).

4) **Pregnant Women**

- Should receive special consideration since infants of mothers who become symptomatic with pertussis up to three weeks before labour have an extremely high risk of disease (10).
- Pregnant women at 36 weeks or more gestation should receive chemoprophylaxis regardless of the setting of exposure (10).
- Those under 36 weeks gestation should receive chemoprophylaxis only in selected settings as described above (10).
- If chemoprophylaxis is not completed by the time of delivery, it should be continued for the mother and started for the newborn afterwards (10).

Asymptomatic Contacts: Regardless of setting, activity restriction is not warranted (10).

Symptomatic Contacts: Symptomatic contacts (cough) should be investigated by a physician (including nasopharyngeal culture) (10). If individuals are diagnosed as cases of pertussis, treatment and exclusion are as outlined above under **Management of Cases**.

Management of Outbreaks

- Vaccination is not recommended for outbreak management, but the opportunity should be taken to update the immunization status of contacts if required (9).
- Currently only the combined acellular pertussis vaccine (Tdap) is available for adolescents and adults. In the past, a minimum five-year interval was recommended between doses for the diphtheria/tetanus toxoid. There had been concern about giving extra doses of the diphtheria/tetanus toxoid to individuals who had recently received their 14-16 year dT (diphtheria tetanus) booster shot (39). However, NACI recently concluded that there was no evidence of increased risk of severe adverse events for Canadian adolescents after receiving diphtheria and tetanus-toxoid containing vaccines at intervals of less than five years (39). See Tdap schedule under **Contact Management**.

Preventive Measures

Vaccination: The main purpose of pertussis vaccination is to reduce the incidence and severity of the disease among young children (5). As estimated from clinical trials, the efficacy of the acellular pertussis vaccine currently used in Canada is about 85 per cent (9).

- Please refer to NACI and the current *Canadian Immunization Guide* (13) for information on routine childhood immunization with pertussis vaccine.
- As protection following pertussis vaccination wanes after six to 12 years in industrialized countries (14), routine use of the acellular pertussis vaccine in adolescents and adults will likely reduce the overall disease burden and transmission to children (40). NACI recommends that all Canadian adults

receive a single dose of Tdap vaccine instead of a tetanus-diphtheria booster (19). See vaccine schedule for Tdap in children seven years of age or older under **Contact Management**.

- Vaccination of pregnant women has been proposed as a strategy to protect infants from pertussis passively before they receive active vaccination; however, data to support the safety and efficacy of maternal vaccination are lacking (33).
- Acellular pertussis vaccines do not protect against infection by *B. parapertussis* (8).

Education: Educate the public, particularly parents of infants, about the dangers of whooping cough and the advantages of initiating immunization at two months of age and adhering to the immunization schedule (41).

Additional Resources

Information for Health Professionals

- Public Health Agency of Canada. National Consensus Conference on Pertussis (2002). *Canada Communicable Disease Report* 2003; Volume 29S3: 1-39.
- *Canadian Immunization Guide 7th edition*, Public Health Agency of Canada. Available at www.phac-aspc.gc.ca/publicat/cig-gci/

Information for the Public

- Fact sheet on Tetanus, Diphtheria, Acellular Pertussis (Tdap) available from Material Distribution Agency (MDA), telephone (204) 945-0570, fax (204) 942-6212 or e-mail: InfoResources@gov.mb.ca

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